A COMPARATIVE STUDY OF SPOT URINE PROTEIN CREATININE RATIO WITH 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA

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CERTIFICATE

This is to certify that the dissertation titled **"A COMPARATIVE STUDY OF SPOT URINE PROTEIN CREATININE RATIO WITH 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA"** submitted by Dr. G. Selvanandhini to the Faculty of Obstetrics and Gynaecology, the Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.D. Degree (Obstetrics and Gynaecology) is a bonafide research work carried out by her under our direct supervision and guidance.

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CONTENTS

INTRODUCTION

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and prenatal morbidity and mortality worldwide. In the developing countries, they rank second only to anemia, with approximately 5 to 10 per cent of all pregnancies being complicated from some form of hypertensive disease.

Hypertensive disorders of pregnancy cover a spectrum of conditions, of which preeclampsia poses a great risk, complicating approximately 5 – 8 % of all pregnancies.

Preeclampsia is best described as a pregnancy-specific syndrome that can affect virtually every organ system. Preeclampsia is defined as the development of hypertension and proteinuria for the first time after mid pregnancy. Although preeclampsia is much more than simply gestational hypertension with proteinuria, appearance of proteinuria remains an important diagnostic criterion. Proteinuria is the surrogate objective marker that defines the systemwide endothelial leak, which characterizes the preeclampsia syndrome.

Obstetricians currently rely on the 24 hour urine collection for determination of proteinuria. However, 24 hour urine collection is cumbersome, both for the patient and the staff handling the urine collection and is subject to error due to inaccurate timing and / or incompleteness. Further, there is a delay of 24 hours from the time of collection till the diagnosis is made.

A more rapid test capable of accurately predicting the results of a 24 hour urine collection would be valuable. An alternative method for the quantitative evaluation of proteinuria is the measurement of protein to creatinine ratio in a spot urine sample. Clinical utility of urine protein to creatinine ratio as a substitute of 24 hour urine protein excretion for significant proteinuria in patients with preeclampsia still remains unclear. Some investigators have proposed the use of spot urine protein to creatinine ratio. However, there are some reports with conflicting results, and the variability in cut off values between studies does not allow a uniform recommendation.

REVIEW OF LITERATURE

Hypertensive disorders complicate 5 to 10 per cent of all pregnancies and together they form one member of a deadly triad, along with hemorrhage and infection that contribute greatly to maternal and prenatal morbidity and mortality rates. How pregnancy incites or aggravates hypertension remains unsolved despite decades of intensive research. Indeed, hypertensive disorders remain among the most significant and intriguing unsolved problems in obstetrics.

Terminology and Classification [1]

Although many classification schemes have been proposed, the scheme of the Working Group of the NHBPEP – National High Blood Pressure Education Programme (2000) is widely followed. The Working Group classification of hypertensive disorders complicating pregnancy describes four types of hypertensive disease:

1. Gestational hypertension
2. Preeclampsia and eclampsia syndrome

3. Preeclampsia syndrome superimposed on chronic hypertension
4. Chronic hypertension

Hypertension

Hypertension is diagnosed empirically when appropriately taken blood pressure exceeds 140 mm of Hg systolic or 90 mm of Hg diastolic. Korotkoft phase V is used to define the diastolic pressure. The incremental increase from mid pregnancy values by 30 mm of Hg systolic or 15 mm of Hg diastolic pressure used in the past as a diagnostic criterion is no longer recommended because recent evidence shows that such women are not likely to experience increased adverse pregnancy outcomes [8, 9].

Proteinuria

Significant proteinuria is defined as the urinary excretion of 300 mg/l or more of proteinuria in a 24 hour urine collection or persistent 30 mg/dl (1+) on dipstick testing for proteinuria in random urine samples.

Gestational hypertension

The diagnosis of gestational hypertension is made in women, who develop non proteinuric hypertension after mid pregnancy, and the blood pressure returns to normal by 12 weeks post partum and the final diagnosis is made post partum.

Preeclampsia

The diagnosis of preeclampsia is made by the occurrence of hypertension along with significant proteinuria after 20 weeks of gestation on a previously normotensive and non proteinuric pregnant woman.

Eclampsia

The onset of convulsions in women with preeclampsia that cannot be attributed to other causes is termed eclampsia.

Superimposed preeclampsia on chronic hypertension

It is defined by the new onset proteinuria in a hypertensive woman, but no proteinuria before 20 weeks of gestation or a sudden increase in proteinuria or blood pressure or platelet count

of less than 100,000/µl in a woman with hypertension and proteinuria before two weeks of gestation.

Chronic Hypertension

A diagnosis of chronic hypertension complicating pregnancy is made when there is a prepregnancy hypertension or hypertension diagnosed before 20 weeks of gestation not attributable to gestational trophoblastic disease or hypertension diagnosed after 20 weeks of gestation, which persists after 12 weeks post partum.

Incidence and Predisposing Factors

Hypertension disorders of pregnancy complicate about 5 to 10 per cent of all pregnancies with 70 per cent of them gestational hypertension, preeclampsia or eclampsia and 30 per cent being chronic hypertension complicating pregnancy [6, 7].

The incidence is influenced by age, family and genetic factors.

Preeclampsia is a disease of young primigravidae and accordingly the incidence is higher in this group. In one study,

among 2434 singleton pregnancies, the incidence was 14.1 per cent in primigravida *versus* 5.7 in multipara [10].

Preeclampsia is more likely to occur at both extremes of reproductive age, but is greater in women younger than 20 years of age. The increased incidence in patients older than 35 years probably reflects undiagnosed chronic hypertension with superimposed preeclampsia.

Primipaternity is also believed to be a risk factor in preeclampsia [11]. Unprotected sexual cohabitation for longer than six months was found to decrease the risk of preeclampsia [11, 12].

The incidence was also increased in patients pregnant with twins (13%) [13] and the incidence was unrelated to zygosity [14].

The incidence is also increased in patients who had preeclampsia in previous pregnancy[15], the probability of recurrence being approximately 30 % and this increases in an inverse relationship to the gestational age at which the patient developed the disease.

Other risk factors include pregestational diabetes, vascular or connective tissue disease, nephropathy, antiphospholipid antibody syndrome, obesity, and family history [16, 17].

Although smoking during pregnancy causes a variety of adverse pregnancy outcomes, ironically, it has consistently been associated with reduced risk of hypertension during pregnancy [18].

Preeclampsia

The minimum criteria for diagnosis of preeclampsia are new onset of hypertension and proteinuria in a pregnant woman after 20 weeks of gestation. The following are the indicators of the severe preeclampsia [1]:

1. Systolic blood pressure of ≥ 160 mm Hg or diastolic blood pressure of ≥ 110 mm of Hg
2. Proteinuria of 5 g or higher in a 24 hour urine specimen or 3+ or greater on dipstick testing of two random urine samples collected at least four hours apart.
3. Oliguria of less than 500 ml in 24 hours
4. Cerebral or visual disturbances

5. Pulmonary edema or cyanosis

6. Right upper quadrant or epigastric pain

7. Impaired liver function

8. Fetal growth restriction

9. Thrombocytopenia

Etiopathogenesis

The exact etiology of preeclampsia is unknown. Several theories have been proposed over the years, most of which have not withstood the test of time. Some of these failed to stand to further investigations, while others yielded conflicting results in different studies, and none could explain all the changes in this condition. As Boyd stated preeclampsia remains “die krankheit der theorien” – the disease of theories [4].

Some of the currently considered factors in the causation of preeclampsia are:

1 Abnormal placentation

In preeclampsia, there is an incomplete trophoblastic invasion of the uterine spiral arterioles resulting in a smaller vessel caliber

with a high resistance to flow. It is likely that the abnormally narrow arterioles impair the placental blood flow. Diminished perfusion and a hypoxic environment eventually lead to release of placental debris that incites a systemic inflammatory response.

2 Endothelial dysfunction

Endothelial dysfunction is a central feature in preeclampsia resulting in activation of coagulation cascade and loss of vascular integrity. Biomarkers of endothelial dysfunction such as plasma fibronectin and thrombomodulin are elevated in preeclamptic pregnancies even before the clinical syndrome manifests, suggesting that endothelial abnormalities are the cause of preeclampsia and not its effect [19].

3 Immunological factors

Loss or dysregulation of maternal immune tolerance to paternally derived placental and fetal antigens is another theory cited to account for the preeclamptic syndrome. Certainly the histological changes at the maternal placental interface are suggestive of acute graft rejection [20]. There are inferential data that suggest an immune mediated disorder, which include:

i. The risk of preeclampsia is appreciably enhanced in circumstances in which formation of blocking autoantibodies to placental antigenic sites might be impaired. In this scenario, the first pregnancy would carry a higher risk [21].

ii. Tolerance dysfunction might also explain an increased risk when the placental antigenic load is increased, that is, with two sets of paternal chromosomes – “a double dose”. For example molar pregnancies have a higher incidence of preeclampsia.

iii. Conversely, women previously exposed to paternal antigens, such as a prior pregnancy with the same but not different partner are immunized against preeclampsia [11,12].

4 Genetic predisposition

A variety of genetic associations to preeclampsia have been recognized. The incident risk of preeclampsia is 20 - 40 % for daughters of preeclamptic women, 11 – 17 % for sisters of preeclamptic women and 22 – 47 % in twins [22]. The hereditary predisposition likely is the result of interactions of literally hundreds of inherited genes – both maternal and paternal. More than 70

genes have been studied for their possible association with preeclampsia. Seven of these have been widely investigated and are listed below.

Genes Frequently Studied for their Association with Preeclampsia Syndrome

Gene (polymorphism)	Function affected	Chromosome	Biological Association
MTHFR (677T)	Methyl tetrahydro-folate reductase	1p 36 – 3	Vascular disease
F 5 (Leiden)	Factor V_{Leiden}	1 q 2 3	Thrombophilia - may coexist with other thrombophilic genes
AGT (M 235 T)	Angiotensinogen	1 q 42 – q 43	Blood pressure regulation, linked to essential hypertension
HLA (various)	Human leukocyte antigen	6 p 21. 3	Immunity

Gene (polymorphism)	Function affected	Chromosome	Biological Association
N O S 3 (Glu 298 Asp)	Endothelial nitric oxide	7q 3 6	Vascular endothelial function
F 2 (G20210 A)	Prothrombin (Factor II)	11 p 11 q – 12	Coagulation – weakly associated, studied with other thrombophilic genes
ACE (I / D^{at} Intron 16)	Angiotensin converting enzyme	17q 2 3	Blood pressure regulation

Adapted from Ward and Lindheimer, 2009 [22]

5 Oxidative stress

Although there is growing evidence indicating the increased risk of preeclampsia in women with elevated levels of oxidized low density lipoproteins and triglycerides, the causal relations of lipid peroxidation in the pathogenesis of preeclampsia is not clear. Cytokines like tumour necrosis factor α, and the interleukins may

contribute to oxidative stress associated with preeclampsia. This is characterized by reactive oxygen species and free radicals that lead to the formation of self propagating lipid peroxides. These in turn generate highly toxic radicals that injure endothelial cells, modify their nitric oxide production, and interfere with prostaglandin balance [23].

The observations on the effect of oxidative stress on preeclampsia have given rise to increased interest on the potential benefits of antioxidants to prevent preeclampsia. However, dietary supplementation with the antioxidants to prevent preeclampsia has, thus far proven unsuccessful.

6 Role of vasoactive agents

1) Renin – Angiotensin – Aldosterone System

In normal pregnancy, all the elements of this system, i.e. renin activity, plasma renin concentration, and angiotensin II levels increase. However the pregnant woman displays reduced responsiveness to the effects of angiotensin II [24].

In preeclampsia, plasma renin activity and angiotensin II levels are usually lower than normal throughout the pregnancy. In addition, the refractoriness to angiotensin II is lost as early as mid-trimester in women who are destined to develop preeclampsia [24,25].

2) Protaglandins

A number of prostanoids are thought to be central to the pathophysiology of the preeclampsia syndrome. There is evidence that compared to normal pregnancies, there is an increase in thromboxane A_2 production and a decrease in prostacyclin (PG I_2) resulting in vasoconstriction.

3) Nitric oxide

Nitric oxide is a potent vasodialator produced by the endothelial cells and is the likely compound that maintains the normal low pressure vasodialated state characteristic of the uteroplacental perfusion. The effects of nitric oxide production in preeclampsia are unclear [26,27]. It appears that the syndrome is associated with decreased endothelial nitric oxide synthase expression.

4) Endothelins

Endothelins are potent vasoconstrictors and Endothelin - I is the primary isoform produced by the human endothelium and its levels are increased in preeclampsia [27].

Pathophysiology

Although the cause of preeclampsia still remains unknown, evidence for its manifestation begins early in pregnancy with covert pathophysiological changes that gain momentum across gestation and eventually become clinically apparent.

1 Cardiovascular system

1) Hemodynamic changes

i. Increased cardiac afterload caused by hypertension

ii. Reduced preload as a result of pathologically diminished hypervolemia of pregnancy during preeclampsia

iii. Decreased cardiac output

iv. Endothelial activation with extravasation of intravascular fluid into extravascular space

2) Blood volume

Hemoconcentration is the hallmark of preeclampsia.

2 Hematological system

1) Thrombocytopenia – It is the most commonly identified hematological abnormality in women with preeclampsia. Overt thrombocytopenia- defined by a platelet count of less than 100,000/µl indicates severe disease. After delivery it will usually reach normal level in 3 to 5 days.

2) Hemolysis – severe preeclampsia is frequently accompanied by evidence of hemolysis, which is semiquantified by elevated serum lactate dehydrogenase levels.

3) HELLP syndrome - In addition to hemolysis and thrombocytopenia, it has also become appreciated that elevated serum hepatic transaminase levels were commonly found with severe preeclampsia and were indicators of

hepatocellular necrosis. Weinstein (1992) referred to this combination of events as HELLP syndrome [28].

4) Coagulation – Subtle changes consistent with intravascular coagulation are commonly found in preeclampsia and superimposed preeclampsia [29]. Some of these changes include:

   i. Increased Factor VIII consumption

   ii. Increased levels of fibrinopeptide and fibrin degradation products

   iii. Decreased levels of regulatory proteins – Antithrombin III and protein C and S

   iv. Unless complicated by abruption, plasma fibrinogen levels do not differ remarkably from levels found in normal pregnancy.

5) Other clotting factors

   i. Thrombophilias are clotting factor deficiencies that lend to hypercoagulability and may be associated with early onset preeclampsia [30].

ii. Fibronectin, a glycoprotein associated with vascular endothelial cell basement membrane is elevated in women with preeclampsia, consistent with endothelial injury

3. Volume Homeostasis

1) Endocrine changes

i. Plasma levels of renin, angiotensin II and aldosterone levels decrease substantially with preeclampsia despite decreased blood volume

ii. Vasopressin levels are similar to that in normal pregnant women

iii. Secretion of atrial natriuretic peptide is decreased in women with preeclampsia

2) Fluid and electrolyte changes

i. In women with severe preeclampsia, the volume of extra cellular fluid, manifesting as edema, is usually greater than that of normal pregnant woman

ii. Electrolyte concentrations do not doffer appreciably in women with preeclampsia compared with that of normal pregnant women

4. Kidney

1) Reduced renal perfusion and hence a reduced glomerular filtration rate, probably as a result of increased renal afferent arteriolar resistance [31].

2) Serum creatinine may rise to values seen in non pregnant individuals, i.e. 1 mg/dl.

3) Plasma serum uric acid concentration is typically elevated in preeclampsia, probably as a result of reduction in glomerular filtration rate and due to enhanced tubular reabsorption [32].

4) Proteinuria which is non selective and is due to endothelial injury in the glomeruli.

5) Preeclampsia is associated with hypocalciuria as a result of result of increased tubular reabsorption [33].

6) Anatomical changes – Glomeruli are diffusely enlarged and are avascular termed as 'Glomerular capillary endotheliosis'.

7) Rarely, acute renal failure as a result of acute tubular necrosis may be caused by preeclampsia.

5 Liver

1) Anatomical changes – Subscapular hemorrhages and rarely rupture can occur in preeclampsia. The characteristic lesions are periportal hemorrhages in the periphery of liver.

2) Elevated serum hepatic transaminase levels which along with hemolysis and thrombocytopenia constitute the HELLP syndrome [28].

6 Brain

Brain may show multiple petechial hemorrhages or larger hemorrhages in the cortex, pons or midbrain. The classical microscopic vascular lesions consist of fibrinoid necrosis of the arterial wall and perivascular microinfarcts and hemorrhages.

7 Visual changes and blindness

Scotomata, blurred vision or diplopia are common with severe preeclampsia or eclampsia. Blindness usually

reversible and may arise from three potential regions – visual cortex, lateral geniculate body or retina (ischaemia, infarctation or retinal detachment).

Proteinuria

In non pregnant women, daily urine protein excretion averages 20 – 80 mg/day (with an upper limit of 150mg/day). This is 40 % albumin, 15 – 20 % immunoglobulin (IgG – 5 – 10 %, IgA – 3 % and light chains 5 – 10 %) and remainder is Tamm-Horsfall glycoprotein derived from the tubules and the lower urinary tract [34].

The movement of proteins across the capillary walls in the glomeruli is influenced by the protein size, configuration and charge.

Renal handling of proteins in normal pregnancy

In pregnancy, the renal hemodynamic changes mean that greater quantities of colloids and solute pass by the glomerular barrier per unit time. In addition, there are changes in glomerular permeability and altered tubular reabsorption of filtered proteins that may result in increased excretion of protein. The currently

accepted upper limit of normal is 300 mg/24 hours for total protein excretion [35].

Altered tubular reabsorption in pregnancy can be demonstrated by measuring urinary excretion of low molecular weight proteins which have identical plasma concentration in non pregnant and pregnant women and are freely filtered by glomerulus. These proteins, including Retinal Binding Protein, β-2 microglobulin and α - 1 microglobulin, have been compared with albumin whose excretion is affected by the size and charge permselectivity of the glomerular barrier. Their increased excretion in uncomplicated pregnancy is due to their reduced reabsorption in the proximal tubule [36].

Renal handling of proteins in preeclampsia

Most classification systems for the hypertensive disorders of pregnancy have placed emphasis on the appearance and progression of proteinuria above a threshold of 300 mg/24 hours to separate gestational hypertension from preeclampsia. This threshold, therefore defines significant proteinuria.

In preeclampsia, the glomerular barrier is certainly altered and there is increased excretion of proteins including albumin. When the total protein excretion exceeds 1.0 g/24 hours, the tubular protein reabsorption will be saturated and individual protein excretion rates will be related to their molecular weights. The term selective proteinuria is used when large protein molecules are retained and non selective proteinuria is used when the glomerular barrier looses this ability. In preeclampsia, the proteinuria is considered to be nonselective [37].

The incidence of proteinuria in most populations is about 10 per cent in all pregnant women. Proteinuria can be caused by pregnancy itself, or may exist from before conception. However, as pregnancy may be the first point of contact, preexisting proteinuria may be first diagnosed at this time. Although less prevalent, primary renal disease or renal disease secondary to systemic disorders such as diabetes or essential hypertension may present with proteinuria in pregnancy.

Proteinuria and clinical outcome

Hypertension with proteinuria is clearly associated with increased fetal and maternal mortality, especially if occurring remote from term [38,39,40,41]. In contrast women with mild hypertension without proteinuria have similar outcomes to non-hypertensive women. But, if chronic hypertension is complicated by the development of proteinuria, there is 10 % incidence of placental abruption, a 33 % incidence of growth restriction and a perinatal mortality of up to 24 % [42].

Page et al. in a prospective study of almost 13,000 pregnant women, found that significant proteinuria was associated with an increase in still birth rates, fetal growth restriction and neonatal morbidity, when associated with hypertension [43].

Ferrazzani et al. studying a group of 444 hypertensive women pregnancies where proteinuria was defined as ≥ 1+ by dipstick or ≥ 0.3g/l, noted higher serum uric acid levels, lower birth weights and birth percentiles, and more deliveries before 37 weeks of gestation, if hypertension was associated with proteinuria [42].

Chua and Kidman have reported that when the level of proteinuria exceeds 5 g/24 hours, delivery is usually required within 2 – 3 weeks [44].

There is no evidence to suggest an adverse maternal or fetal outcome in relation to the degree of proteinuria and hence it is the presence of proteinuria that confers increased maternal and perinatal morbidity, not necessarily its severity [9].

In a study by Waugh et al. among 197 pregnant women, it was found that the threshold of 300 mg/24 hours was not predictive of the adverse outcome. They concluded that though 300 mg/24 hours may be above the 95th centile for an obstetric population, it is the threshold of 500 mg/24 hours that is more predictive of an adverse outcome [45].

Assessment of proteinuria

All pregnant women are routinely screened for proteinuria at their first visit and at regular intervals thereafter by heat coagulation test or dipstick test. If the test is negative, clinically significant proteinuria is precluded; but if it is positive, further investigation is necessary.

Heat coagulation test

It is done by adding 3 – 4 drops of acetic acid to the urine after heating. Results are graded depending on the turbidity and hence are subjective. They are associated with a number of false positive and false negative results [3].

Dipstick test

This test is carried out on the first morning specimen of urine, preferably because it tends to be more concentrated and is not affected by postural factors. The dipsticks are more sensitive to albumin than other plasma proteins.

The reactive portion of the stick is coated with a buffered indicator that changes colour in the presence of protein and the test is read after 60 seconds. It is graded as follows [5]:

Trace	-	0.1 g/l
1+	-	0.3 g/l
2+	-	1 g/l
3+	-	3 g/l
4+	-	10 g/l

Dipstick testing is, however, associated with a large number of false positives which can be due to a very concentrated specimen (specific gravity of more than 1.030), alkaline urine, contamination with antiseptics like chlorhexidine or quaternary ammonium compounds or vaginal discharge. False negative results can also occur due to very dilute urine (specific gravity of less than 1.010) [3].

Quantitative assay of proteinuria

Persistent dipstick proteinuria requires further evaluation. Quantitative assay for total proteins excretion is usually performed on timed collections, usually a 24 hour urine specimen.

24 hour urine collection

The 24 hour urine collection for estimation of proteinuria is the gold standard in diagnosis of proteinuria in preeclampsia. Though a reliable indicator of proteinuria, it has the disadvantage of being a cumbersome and time consuming process, subject to collection error and requires patient compliance. Further, there is a delay of 24 hours from the time of collection till the diagnosis is made.

Dipstick urinalysis and 24 hour urinary protein excretion

The primary reason for the dependence upon the dipstick test is the relative low cost and ease with which it can be performed. It is a widely held belief that 1+ proteinuria by dipstick corresponds to 300 mg/24 hours total protein excretion. There are several studies which investigated the relationship between semiquantitative dipstick urine analysis on random voided urine samples and a subsequently collected 24 hour urine sample.

In a study by Meyer et al. among 300 hypertensive women, 66 % of the women had false negative dipstick urinalysis, if significant proteinuria was defined as ≥ 300 mg/24 hours. In the same series they reported a false positive rate of 26 % at the 1+ level [46].

In a study, Brown et al. reported a false negative result of 8 – 18 % and a very high false positive rate of 67 % with 1+ score. They suggested that the dipstick is too sensitive at the 1+ threshold and that as such it is useful for the management of preeclampsia as it will minimize the false negative results (missed proteinuria), but the test will be incorrect at least half of the time [67].

Waugh et al.'s data on 197 hypertensive women, found a high false negative rate of up to 65 % in women with < 1+ proteinuria on dipstick analysis, but had significant proteinuria [47].

All these suggest that the correlation between dipstick urinalysis and 24 hour protein estimation is at best imprecise. False positive results may result in over investigation and intervention whereas the potentially more serious issue of false negative result may place a woman and her pregnancy at risk.

The review of literature thus shows that the accuracy of dipstick urinalysis using a threshold in the prediction of significant proteinuria is poor. It is, however, not possible for dipstick urinalysis to be removed from antenatal care without a viable alternative test to replace it.

Protein to creatinine ratio in spot urine samples

Measurements on random urine samples of the protein to creatinine ratio have been reported to show a good correlation with subsequent 24 hour urine protein estimation in non pregnant populations (renal impairment [48], kidney transplants [49] and diabetes[50]). There has also been good evidence of a strong

correlation between random sample protein to creatinine estimation and subsequent 24 hour protein excretion in hypertensive pregnant population.

In the presence of a stable renal function test, a protein to creatinine ratio of < 0.2 is said to be within normal limits and a protein to creatinine ratio of > 3.5 represents nephrotic range of proteinuria. Studies reasoned out that the ratio of two stable excretion rates (protein and creatinine) minimize the time involved, thus providing a faster estimate of 24 hour protein excretion [51,52].

Leanos-Miranda et al. from their cross-sectional study of 927 hospitalised pregnant women with suspected preeclampsia and 161 pregnant women in whom hypertensive disorders of pregnancy was ruled out for comparison, found that the protein to creatinine ratio and the 24 hour protein excretion were significantly correlated ($r = 0.98$, $p < 0.001$). The protein to creatinine ratio as an indicator of protein excretion of ≥ 300 mg/24 hours was ≥ 0.3. The sensitivity and specificity were 98.2% and 98.8% respectively. The positive and negative predictive values were 97.2% and 99.2%. They concluded that protein to creatinine ratio may be reasonably used as an alternative to the 24 hour urine collection method [53].

In a study by Shahbazian et al. among 81 pregnant women with preeclampsia, there was a strong correlation between the spot protein to creatinine ratio and 24 hour urine protein excretion ($r = 0.84$, $p < 0.001$). The optimal spot protein to creatinine ratio cut off point was 0.20 for 300 mg/24 hours of protein excretion, with a sensitivity, specificity, positive predictive value and negative predictive value of 91.2 %, 87.8 %, 94.4 % and 96.8 %, respectively. The value of less than 0.19 yielded a sensitivity of 100 % for exclusion of preeclampsia [54].

In another study by Nisell et al., there was a close correlation between the albumin to creatinine ratio and 24 hour albumin excretion values ($r = 0.95$, $p < 0.001$) and they concluded that in most cases, the more cumbersome 24 hour urine collection can be replaced by the more convenient albumin to creatinine ratio on the spot urine [55].

Papanna and colleagues in a systematic review, concluded that the random urine protein to creatinine ratio determinations are helpful primarily when they are below 130 – 150 mg/g, in that 300 mg or more proteinuria is unlikely below this threshold. Midrange

protein to creatinine ratio (300 mg/g) had poor sensitivity and specificity, requiring a full 24 hour urine for accurate results [56].

In a study by Wheeler et al., though random spot urine protein to creatinine ratio was strongly correlated with the 24 hour urine protein levels (r = 0.88), it was concluded that the use of spot protein to creatinine ratio was not justified as a substitute for timed collection [57].

In a systematic review, Cote et al. concluded that the spot protein to creatinine ratio is a reasonable “rule out’’ test for detecting proteinuria of 0.3 g/day or more in hypertensive pregnancy [58].

Durnwald and Mercer in their study among 220 women found a poor correlation between the spot urine protein to creatinine ratio and 24 hour urine protein (r^2 = 0.41) and they concluded that protein to creatinine ratio does not exclude adequately the presence of significant proteinuria or predict severe proteinuria and should not be used as an alternative to 24 hour total protein excretion [59].

So the clinical utility of urine protein to creatinine ratio as a substitute of 24 hour urine protein excretion for detecting significant proteinuria still remains unclear. Though some investigators have proposed the use of spot urine protein to creatinine ratio, there are also reports with conflicting results.

In this study, the correlation between the spot urine protein to creatinine ratio and 24 hour urine protein excretion in patients being evaluated for preeclampsia has been studied.

AIM OF THE STUDY

1. To study the correlation between the spot protein to creatinine ratio of a single random sample and 24 hour urine protein excretion in women admitted for evaluation of preeclampsia.

2. To know if spot protein to creatinine ratio would provide accurate quantification of proteinuria in preeclampsia.

MATERIALS AND METHODS

Study period : December 2009 to November 2010

Sample size : 150

Study design : Prospective study

Source of data

One hundred and fifty pregnant women who were admitted for evaluation of preeclampsia were studied prospectively after getting informed written consent. The study was conducted at the Department of Obstetrics & Gynaecology at Govt. R.S.R.M. Lying-in Hospital attached to Stanley Medical College, after getting approval from the Hospital Ethical Committee.

Selection criteria

Inclusion criterion

Pregnant women with preeclampsia, with preeclampsia being defined as systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg on at least two occasions 6 hours apart , accompanied by a proteinuria of ≥ + 1 as detected by dipstick test, after 20 weeks of gestation.

Patients were categorized as severe preeclampsia, if any of the following criteria are met:

Systolic BP ≥ 160 mm Hg

Diastolic BP ≥ 110 mm Hg

Proteinuria of 5 g/24hours or more or persistent 3+ by Dipstick

Oliguria (24 hour urine output < 500 ml)

Cerebral / Visual disturbances

Pulmonary edema

Epigastric / Upper right quadrant pain

Impaired liver function

Thrombocytopenia

IUGR

Elevated serum creatinine level

Exclusion criteria

1. Pre-existing renal disorder – A stable renal function was ascertained by doing Blood urea and Serum creatinine
2. Urinary tract infections – Urine analysis was done for all patients to exclude the presence of microscopic hematuria, casts and bacteriuria.
3. Chronic hypertension
4. Gestational diabetes

5. In addition, woman who delivered their babies during the day of urine collection were excluded.

Procedure

One hundred and fifty patients who satisfied the above criteria were recruited for the study. Informed written consent was obtained from all the patients.

1. A detailed history was taken.
2. General physical and systemic examination was done.
3. The blood pressure was measured with an appropriate size cuff with the patient in an upright position after at least 10 minutes rest. Diastolic BP was determined as the disappearance of sound (Korotkoff Phase V).
4. Complete obstetric examination was done. Per speculum examinations were done to look for any evidence of vaginal infection clinically.
5. Urine microscopy was done to rule out the presence of infection.
6. Proteinuria was assessed in a random sample of urine by the dipstick method. Proteinuria by the dipstick method was graded as follows:

Trace	0.1 g/l
1 +	0.3 g/l
2 +	1 g/l
3 +	3 g/l
4 +	10 g/l

If the dipstick test showed proteinuria of 1+ or more, quantitative tests for proteinuria were carried out.

7. Spot urine protein – creatinine ratio

   A spot midstream sample of urine was collected from all the patients, immediately prior to the beginning of the collection for 24 hour urine protein estimation. The samples were sent to the Biochemistry laboratory where

   a) Urine protein was measured by the sulphosalicylic acid method
   b) Urine creatinine was estimated by Modified Jaffe's method
   c) The urine protein and creatinine ratio was obtained by dividing the urine protein concentration (in mg/dl) by the urine creatinine concentration (in mg/dl)

8. Urine samples were collected for 24 hours (after collecting the specimen for spot test) and the urinary protein excretion in 24 hours was estimated.

9. Normal values for protein excretion

24 hours urine protein (in mg/24 hours)

Not significant	< 300
Clinically significant	> 300
Severe proteinuria	> 5000

Protein creatinine ratio

Not significant	< 0.2
Clinically significant	≥ 0.20

10. Hemoglobin (g/dl), Platelet count, Blood urea, serum creatinine and liver function test (Sr. bilirubin, Sr. proteins (total and albumin), SGOT & SGPT, LDH) were done for all patients.
11. Fundus examination was done for all patients
12. USG and Doppler study was done wherever indicated (suspicion of IUGR)
13. The data thus collected were analyzed using appropriate statistical methods. Descriptive statistics were used for demographic and baseline data and summarized as mean $\pm$ S.D., median and percentage, wherever appropriate.

14. The relationship between the urine protein creatinine ratio and 24 hour protein excretion was assessed with Pearson's correlation test and correlation coefficient was calculated which is expressed as "r".

RESULTS AND ANALYSIS

Table I : Age distribution of subjects

Age (years)	Mild preeclampsia	Severe preeclampsia	Total
< 20	20 (13.33)	15 (10)	35 (23.33)
21 – 30	68 (45.33)	30 (20)	98 (65.33)
> 30	7 (4.67)	10 (6.67)	17 (11.33)
Total	95 (63.33)	55 (36.67)	150 (100)

Figures in parentheses indicate percentage

In this study, it was noticed that majority (65.33 %) of the 150 subjects studied were in the age group of 21 – 30 years (Fig. 1).

Fig. 1 Age distribution of subjects with mild and severe preeclampsia

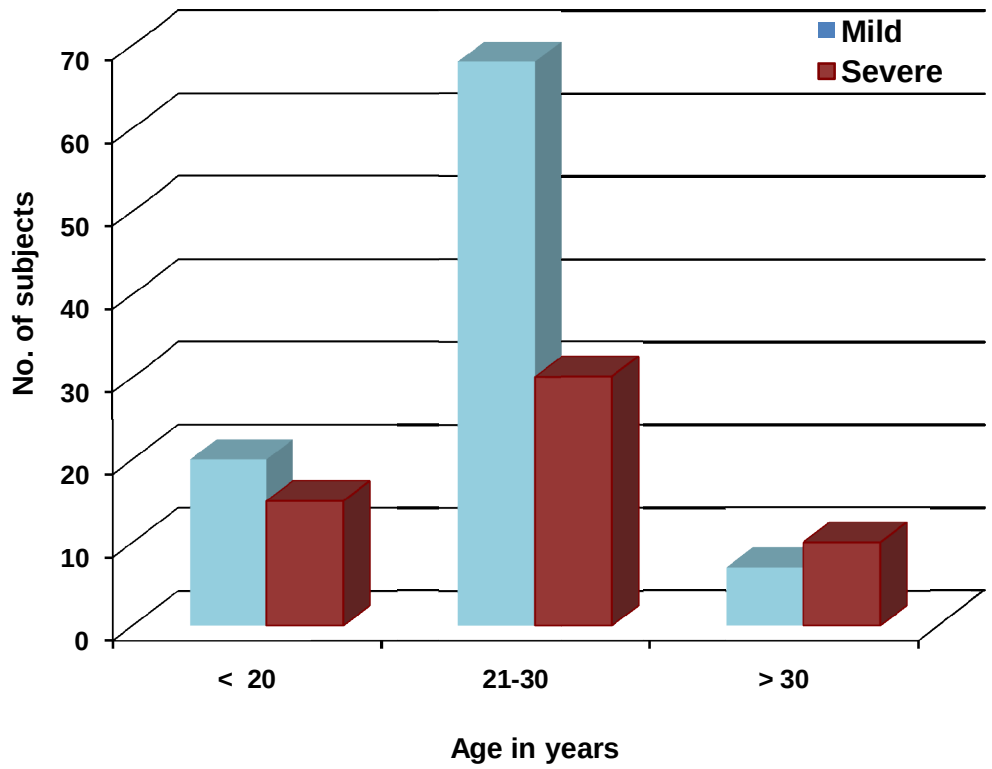


Table II: Distribution of preeclampsia among subjects

Preeclampsia	Frequency	Per cent
Mild	95	63.33
Severe	55	36.67
Total	150	100

It was noticed in this study that of the 150 subjects studied, 63.33% were having mild preeclampsia and 36.67% had severe preeclampsia (Fig. 2).

Fig. 2 Pie chart showing distribution of preeclampsia among subjects

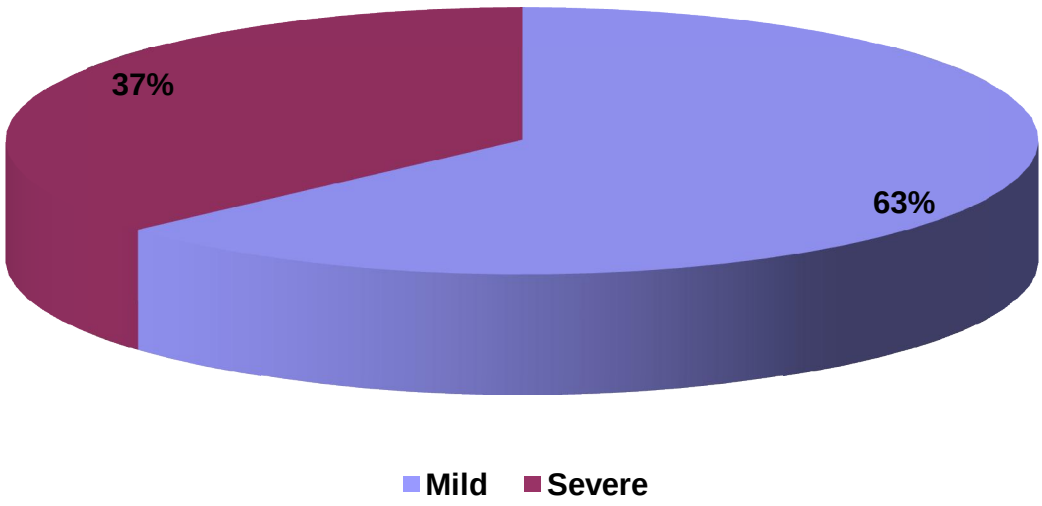


Table III: Paritywise distribution of subjects

Gravida	Preeclampsia		Total
	Mild	Severe	
Primi	49 (32.67)	37 (24.67)	86 (57.33)
Multi	46 (30.67)	18 (12.00)	64 (42.67)
Total	95 (63.33)	55 (36.67)	150 (100)

Figures in parentheses indicate percentage

It is observed in this study that the incidence of pre-eclampsia in primigravida was 57.33% and multigravida was 42.67% (Fig. 3).

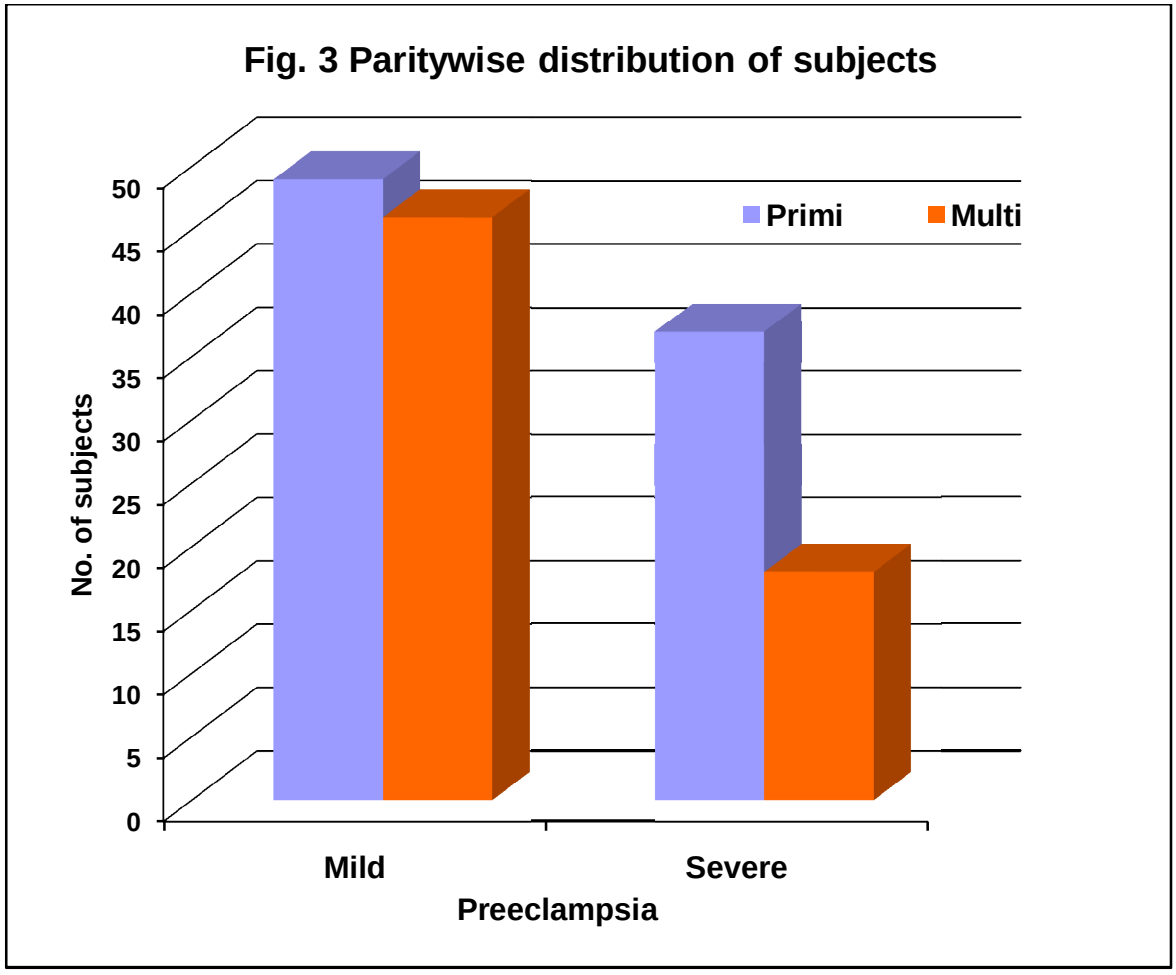


Fig. 3 Paritywise distribution of subjects
No. of subjects
50
45
40
35
30
25
20
15
10
5
0
Primi
Multi
Mild
Severe
Preeclampsia

Table IV: Distribution of subjects as per gestational age

Gestational age (wks.)	Preeclampsia		Total
	Mild	Severe	
20 – 28 weeks	6 (4.00)	5 (3.33)	11 (7.33)
28 – 36 weeks	47 (31.33)	33 (22.00)	80 (53.33)
≥ 37 weeks	42 (28.00)	17 (11.33)	59 (39.33)
Total	95 (63.33)	55 (36.67)	150 (100)

Figures in parentheses indicate percentage

It was observed that, out of 150 subjects majority (53.33 %) were between 28 – 36 weeks. Severe preeclampsia was also found to be most common in this group accounting for 33 of 55 (60%) severe cases (Fig. 4).

Fig. 4 Distribution of subjects as per gestational age

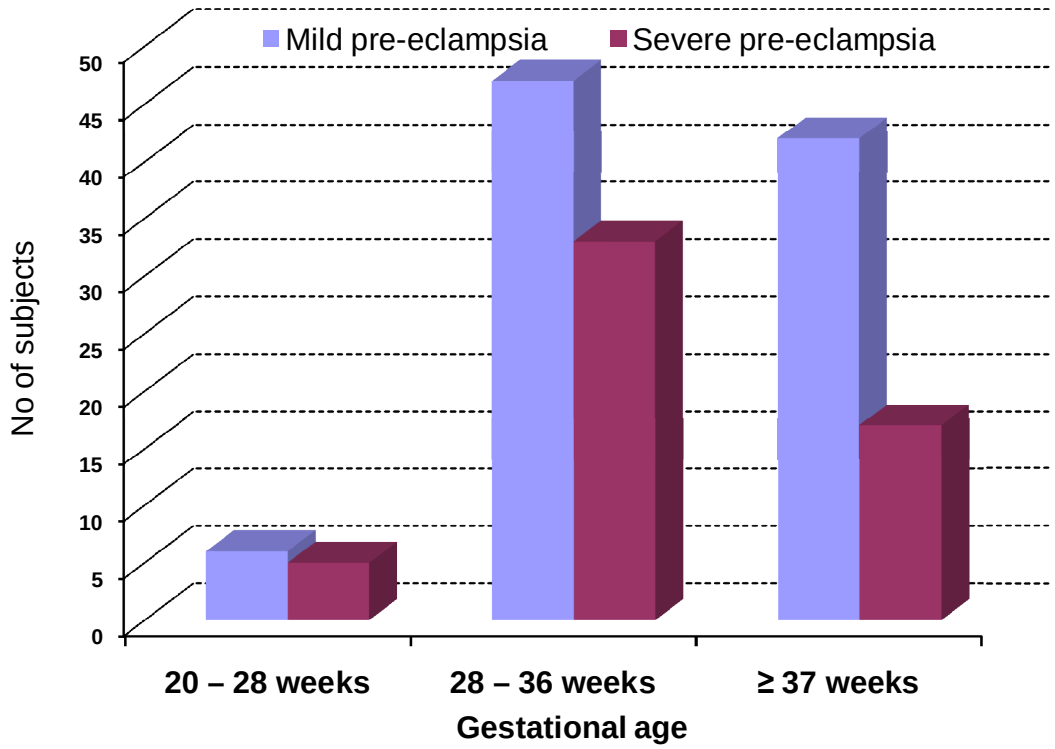


Table V: Summary statistics of different parameters*

Variables	Mean	SD	SE	Minimum	Maximum
Age in years	24.20	4.75	0.388	18	37
POG in weeks	34.62	3.69	0.301	24	40
Sys. BP in mm of Hg	144.95	9.65	0.788	130	170
Dia. BP in mm of Hg	93.99	7.63	0.623	80	110
24 hours urine protein in mg/day	925.02	1077.28	87.39	132	7800
Protein creatinine ratio	1.52	1.46	0.119	0.13	11.39

* The number of subjects is 150

Box plot analysis showed that values with more than 2000 mg/24 hour urine extraction were outliers (Fig. 5).

Box plot analysis also showed that spot protein creatinine ratios above 2.5 are extreme values (Fig. 6).

Fig. 5. Box plot showing 24 hour urine protein excretion (All data)

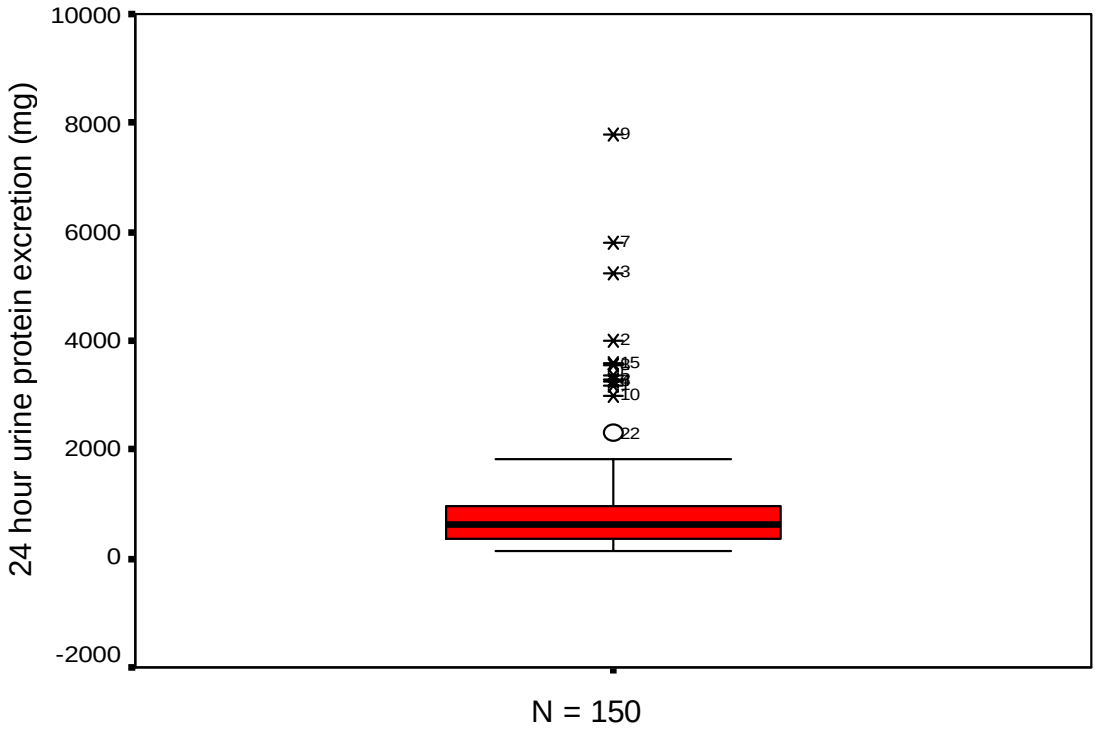


Fig. 6. Box plot showing spot protein creatinine ratio (All data)

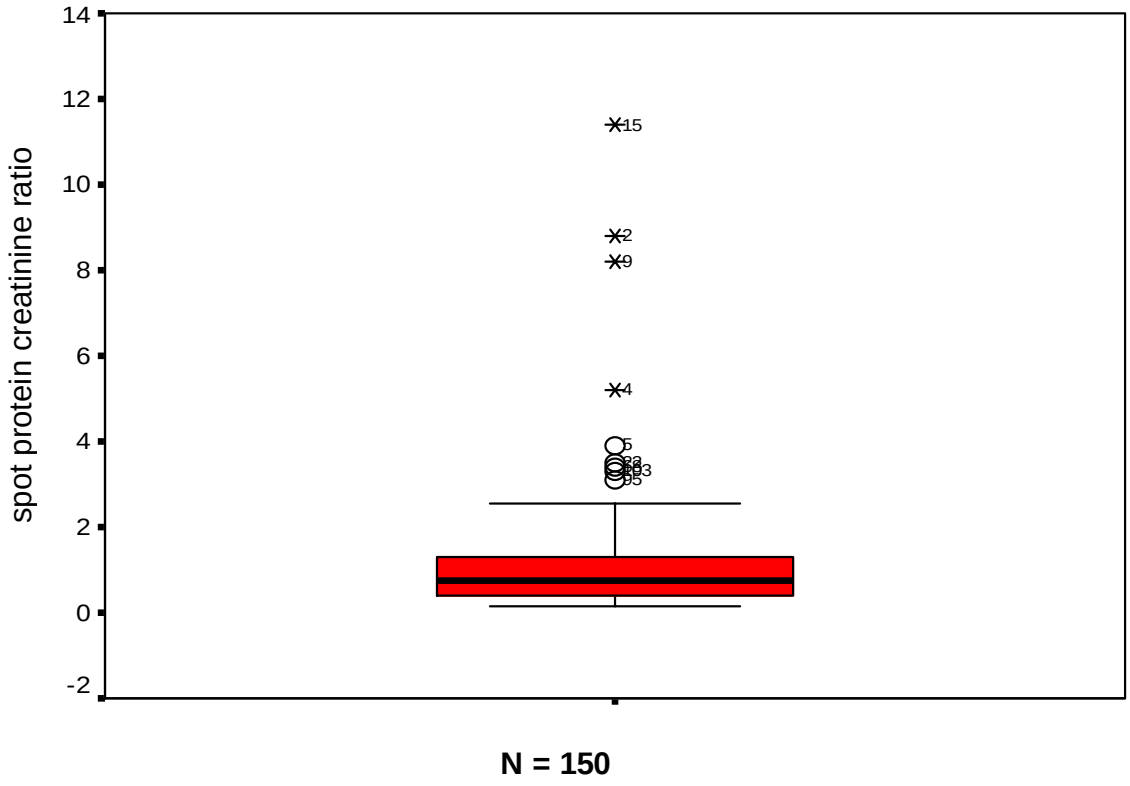


Table VI: Comparison of urinary dipstick against 24 hours urine protein

Dipstick	24 hours urine protein (mg/day)			Total
	< 300	300 - 2000	>2000	
1 +	29	66	-	95
2 +	2	33	1	36
3 +	-	6	9	15
4 +	-	2	2	4
Total	31	107	12	150

The box plot analysis of 24 hour urine protein extraction at different dipstick readings (Fig. 7) showed that at dipstick readings at 1+ and 4+ the median line is almost in the centre of the box, indicating more or less normal distribution of these values. However at the dipstick values of 2+ and 3+ there is a skewed distribution.

Fig. 7. Box plot analysis of 24 hour urine protein excretion at different dipstick values

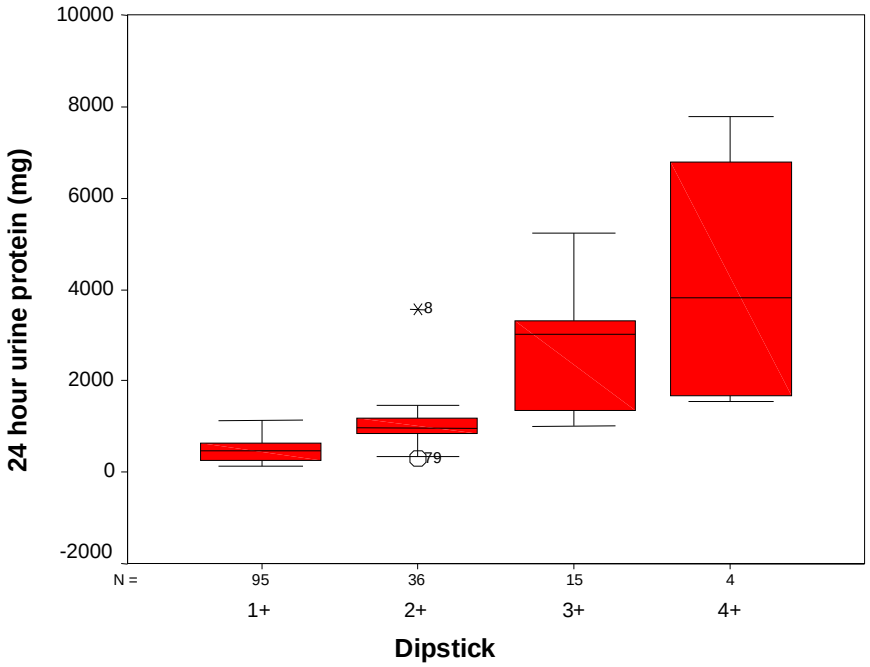


Table VII : Comparison of urinary dipstick against protein creatinine ratio

P/C ratio	Dipstick				Total
	1 +	2 +	3 +	4 +	
< 0.2	12	1	-	-	13
≥ 0.2	83	35	15	4	137
Total	95	36	15	4	150

The box plot analysis of spot protein creatinine ratio at different dipstick readings (Fig. 8) showed that the distribution of spot protein creatinine ratios is skewed at all dipstick readings and more values were in the upper quartile of the median. However the degree of skewness was less in the dipstick value of 1+.

Fig. 8. Box plot analysis spot protein creatinine ratio at different dipstick values

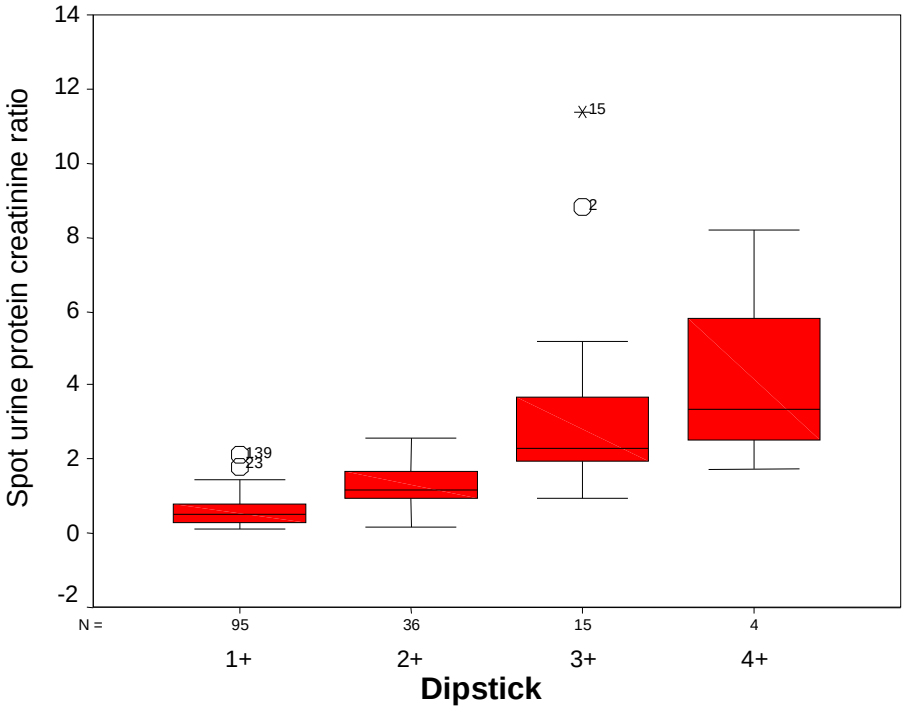


Table VIII : Comparison of 24 hour urine protein and spot urine protein creatinine ratio

Spot PCR	24 hours urine protein mg/day			Total
	< 300	300 – 2000	> 2000	
< 0.2	13	2	-	15
≥ 0.2	18	105	12	135
Total	31	107	12	150

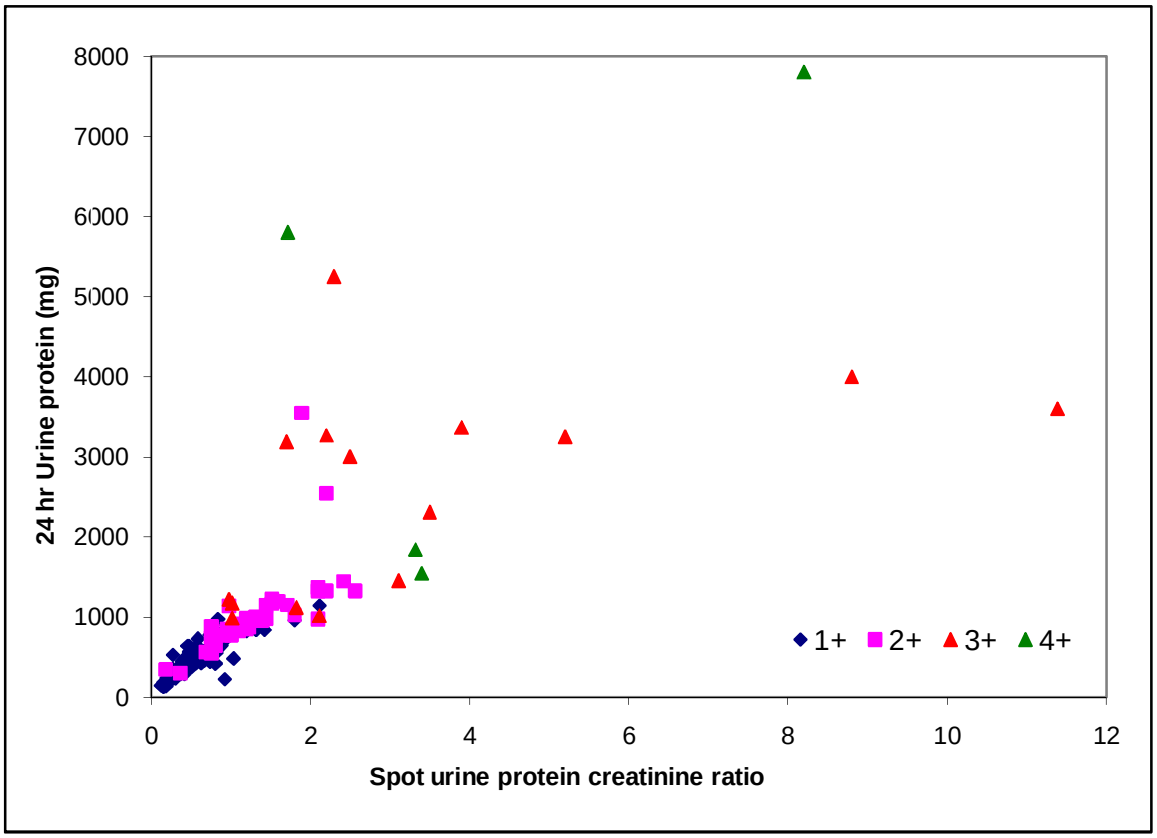
Correlation coefficient between protein/creatinine ratio and 24 hour urinary protein

Karl Pearson's correlation between	Correlation coefficient "r"	P value
PCR and 24 hours urine protein	0.756	0.01

A fair correlation of r = 0.756 was observed between the 24 hours urine protein and spot urine protein-creatinine ratio among the 150 subjects, which was significant at a P value of < 0.01.

The scatter plot shown in Figure 9 indicates a good linear relationship between the two variables.

Fig.9. Scatter plot showing the distribution of 24 hour urine protein (mg) and spot urine protein creatinine ratio (all values)



When only the data for 24 hours urine protein < 2000 is analyzed, the simple linear correlation between 24 hours urine protein and spot urine protein creatinine ratio a shows better linear relationship (Fig. 10) and the “r” value is 0.914 which is highly significant at 0.001 probability level. This is also illustrated by the Figure 11 showing linear and quadratic relationship between spot urine protein ratio and 24 hour urine protein as well as the observed values.

The linear relationship of 24 hour UP (y) on SPCRATIO (x) is given by the following relationship:

a. 24 hour UP = 206.58 + 509.42 * SPCRATIO with a high coefficient of determination (83%)
b. The Students’ t-test indicates that the regression coefficient is highly significant (P=0.01)
c. The estimated coefficients of the above model can be expressed as:

    Constant ‘a’ = 206.58 ± 21.10

    Regr.Coeff ‘b’ = 509.42 ± 19.40,

    where the values after the operator ± are Standard Errors of the respective coefficients

Fig. 10. Scatter plot showing the distribution of 24 hour urine protein and spot urine protein creatinine ratio (for 24 hour urine protein values < 2000)

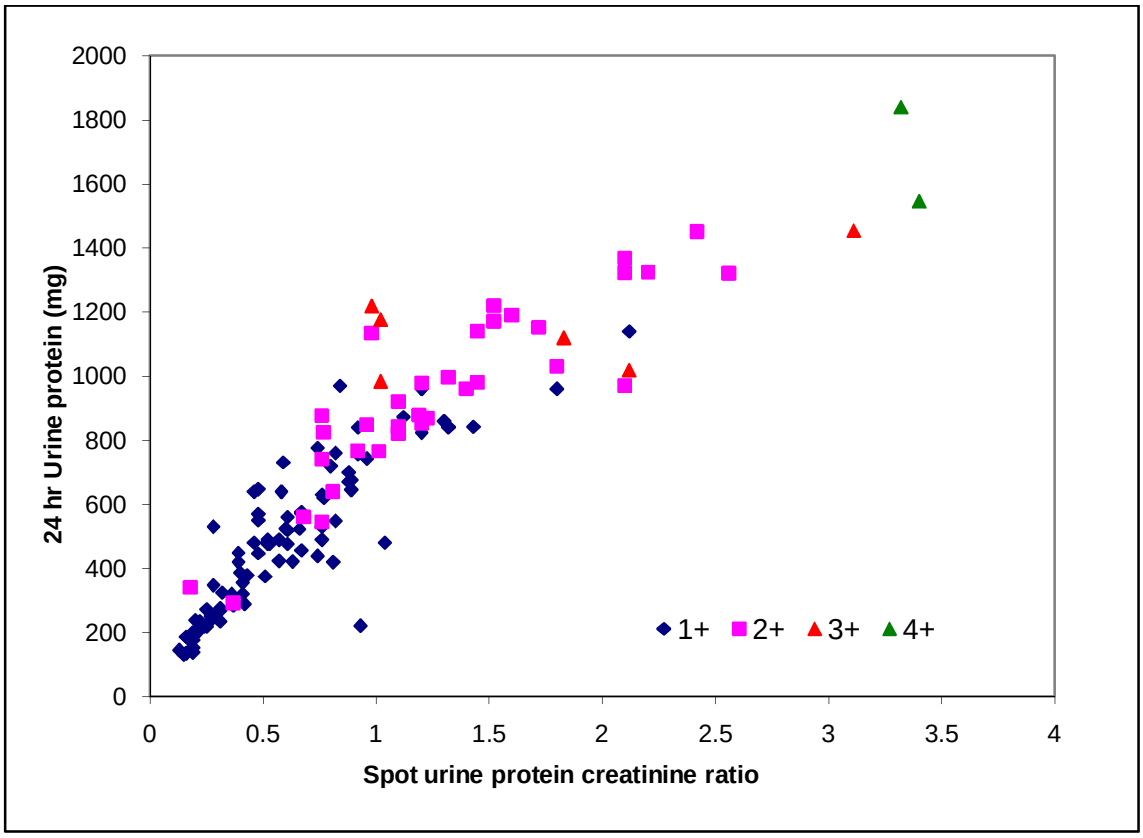
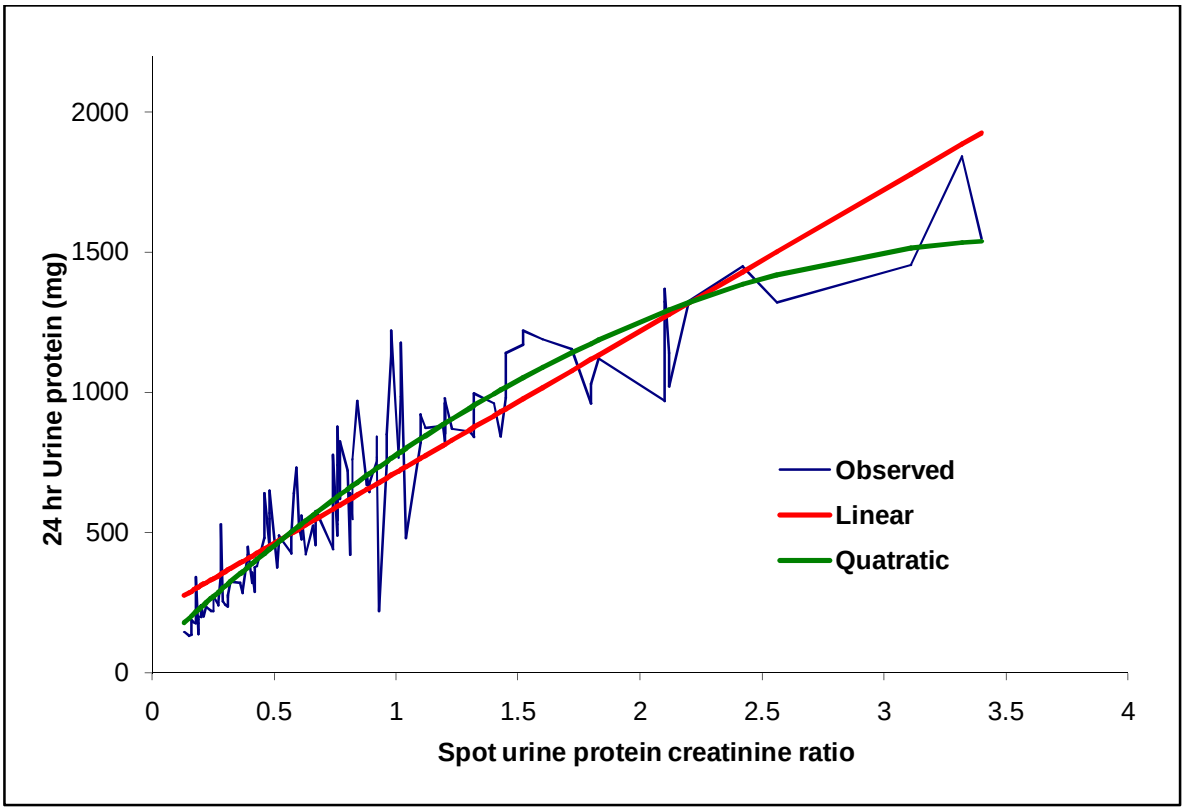


Fig. 11 Graph showing linear and quadratic relationship between spot urine protein ratio and 24 hour urine protein



The graphical presentation of the linear model fit is shown in the following figure (green line). A quadratic model fit is also shown (the red colored curve). Since the quadratic model does not give appreciable increase in coefficient of determination (R^2), the linear model is sufficient for all practical purposes.

For a given value of X (Spot protein creatinine ratio), the Y (24 hour urine protein extraction) value can be estimated from the equation (a) above, so also for a given Y (24 hour urine protein extraction), the corresponding projection on X can be estimated. So for a value of 24 hour urine protein extraction = 300, the Spot protein creatinine ratio is estimated to be: **0.1834.**

With the protein creatinine ratio of 0.2 taken as the threshold to detect significant proteinuria, the sensitivity and specificity were 100% and 45% respectively and the positive and negative predictive value were 86.9% and 100% respectively.

DISCUSSION

Measurement of proteinuria is one of the most routinely undertaken laboratory procedures. It is mandatory in evaluating women with hypertensive disorders of pregnancy, and is necessary to establish the diagnosis of preeclampsia, as well as its severity. Urinary protein excretion during a 24 hour period, however, is considered to be cumbersome and subject to error due to inadequate collection.

This study was conducted to evaluate the correlation between 24 hour urine protein excretion and spot protein creatinine ratio on random urine samples and to determine its accuracy. A rapid and accurate test may avoid the inconvenience for the patient and will also avoid the delay in diagnosis and management.

This study was limited to the hospitalised nonambulatory patients. Since the protein excretion is affected by postural changes, being higher in the standing than in supine position, the ambulatory status of the patient is important while interpreting the results.

In this study of 150 preeclamptic women, the socio-demographic variables shows that the peak age range was 21 - 30 years with the mean age being 24.20 years. The peak age of 21 – 30 years may be reflective of the fact that most first deliveries in this environment occur at that age and not necessarily of any special contribution of this age bracket to the etiology of the disease.

This study included a large number of patients with mild preeclampsia (63.33%). Primigravidae contributed the commonest parity (57.33 %). Primigravidae have been demonstrated by numerous workers to be at high risk of developing preeclampsia. The mean gestational age of the patients under study was 34.62 weeks.

We found a fair correlation in our study, when the 24 hour urine protein and the random urine protein creatinine ratios were correlated, with correlation relation coefficient, $r = 0.756$ and p value being significant at < 0.01, when all the observations were considered.

The correlation was better at r = 0.914 and p < 0.001, for lesser degrees of proteinuria i.e. < 2000 mg/24 hours. But when the correlation was computed for higher degrees of proteinuria i.e. > 2000 mg/24 hours, there was very poor correlation, r – negative, and not statistically significant.

Boler and associates studied the two parameters in 54 patients. Excellent correlation was achieved (r = 0.9935, p <0.001) between the two, and this was achieved for normal pregnancies, hypertensive pregnancies and multiple gestation. They however did not specify the number of patients with preeclampsia. In patients with proteinuria of more than 1 g/24 hours, there were variations in the results [62]. Similarly, the study conducted by Jaschevatzky and associates on 35 preeclamptic patients and 70 healthy patients found close correlation (r = 0.9278, p < 0.001) between 24 hour proteinuria and random urinary protein creatinine ratio. However, in patients with proteinuria greater than 2 g, the degree of correlation decreased [65]. In both the studies, the sample size was smaller than in this study, and predictive values of the tests were not available.

In a study by Torng et al in 2001 to determine whether urine protein/creatinine ratio can be used as a predictor for 24 hour protein excretion in transplant patients, a good correlation could be established between the two variables at 0.5 – 2.0 g/day of proteinuria. But the precision and positive predictive value decreased as proteinuria increased >3g/day [68].

This variation in the results at severe degrees of proteinuria indicates the need for careful interpretation of the results especially when clinical decisions are to be based on them.

Out of 150 patients, 12 patients had proteinuria greater than 2 g/24 hours and only 3 patients had proteinuria of greater than 5 g/24 hours, which is an inadequacy of this study. A poor degree of correlation at severe degrees of proteinuria could probably be due to the low prevalence of subjects with this range of proteinuria.

Since the present study included women only with a stable renal function, our study supports the use of the protein/creatinine ratio in women with normal renal function.

But Robert et al [61] in 1997 and Quadri et al [51] in 1994 have proved in their studies that the protein/creatinine ratios are

independent of renal function and reliable even in the presence of underlying renal disease and have advocated their use to monitor renal function in pregnancy.

Given below is a table which shows the results of some similar studies in comparison with the present study.

Studies	**Correlation Coefficient (r)**	**p-value**
Nisell et al. [55]	0.95	< 0.001
Yamasmit et al.[60]	0.929	< 0.001
Robert et al. [61]	0.94	< 0.001
Boler et al. [62]	0.99	< 0.001
Rodriguez - Thompson et al.[63]	0.80	< 0.001
Young et al. [64]	0.80	< 0.001
Jaschevatzky et al.[65]	0.92	< 0.001
Shahbazian et al. [54]	0.84	< 0.001
Bansal et al.[66]	0.83	=0.000
Present study	0.756	<0.01

Research in future should be focused on the evaluation of clinical outcomes and the cost effectiveness of the use of a random urinary protein creatinine ratio for prediction of significant proteinuria. In addition, studying the test in an outpatient basis should be further considered in order to apply it in ambulatory management of preeclamptic patient. We suggest the test be done also in severely preeclamptic women, as they tend to excrete greater amounts of protein, in order to determine a cutoff value for prediction of the 24 hour protein excretion greater than 5 g.

SUMMARY

The objective of the study was to know if a spot protein/creatinine ratio would provide an accurate quantification of proteinuria and whether it can replace the use of the 24 hour urine protein in preeclamptic women.

One hundred and fifty women with pre-eclampsia were recruited for the study. A stable renal function was ascertained by estimating serum creatinine and blood urea levels. The patients were instructed to collect the 24 hour urine starting from the second urine sample in the morning till the first urine sample the next day morning. A single voided urine specimen was obtained before the start of 24 hour collection for determination of the protein/creatinine ratio. The urine protein was measured using sulphosalicylic acid method. Urine creatinine was measured using modification of Jaffe's reaction which is commonly used to estimate creatinine. Urine protein (mg/ml) was divided by urine creatinine (mg/ml) to obtain the ratio. Statistical method used was the Pearson's correlation coefficient.

In our study results were:

- A good correlation existed between the two variables with r = 0.756 with a highly significant p value = <0.01 when all the observations were considered.
- When only lesser degrees of proteinuria were taken, the correlation was good at r = 0.914, p <0.001.
- The correlation at high levels of proteinuria was very poor, having a negative value and statistically insignificant p value.

Hence care should be taken while interpreting the protein/creatinine ratios at severe degrees of proteinuria.

CONCLUSION

Since the level of urinary protein excretion has considerable clinical implications in the course of pregnancy, the early detection of even minor degrees of hyperproteinuria is important.

Dipstick analysis as a screening for proteinuria lacks reliability with a high rate of false positives.

For years, 24 hour urine collection has been the standard for quantitation of proteinuria in the management of women with pre-eclampsia. However, this method is cumbersome, subjective to collection errors, requires good patient compliance and results in the delay in the diagnosis of > 24 hours from the start of collection. Our contention was that the value of the protein/creatinine ratio in a single urine sample is potentially more accurate, because it avoids collection errors and may give more physiologically relevant information.

Quantitating proteinuria in a random sample has found to be far more cost effective and acceptable to the patient than a 24 hour urine collection.

Since preeclampsia is a progressive disease, repeated laboratory examinations to quantitate protieinuria are required. Protein/creatinine ratio has been found to be a superior diagnostic tool compared to the routine urinalysis which would otherwise be used for daily quantitation of proteinuria.

Based on the findings of the present study, we conclude that a random urine protein creatinine ratio predicts the amount of 24 hour urine protein excretion reasonably. This test could be a reasonable alternative to the 24 hour urine collection for detection of significant proteinuria in hospitalised pregnant women with suspected preeclampsia.

PROFORMA FOR STUDY

NAME :

AGE :

IP. NO. :

ADDRESS :

LMP :

EDD :

GESTATIONAL AGE :

PARITY :

ANY H / SUGGESTIVE OF PREECLAMPSIA :

H / O PREECLAMPSIA IN PREVIOUS PREGNANCIES :

FAMILY H / O PREECLAMPSIA :

H / O HYPERTENSION/REAL DISORDERS / DIABETES / UTI

MEDICATIONS: ANTIHYPERTENSIVES :

GENERAL EXAMINATION :

- HEIGHT
- WEIGHT
- ANEMIA
- ICTERUS
- EDEMA
- PULSE
- BP

CVS

RS

OBSTETRIC EXAMINATION :

URINE MICROSCOPY :

URINE PROTEIN BY DIPSTICK TESTING :

24 HOUR URINARY PROTEIN :

SPOT PROTEIN CREATININE RATIO :

BLOOD UREA :

SERUM CREATININE :

HEMATOCRIT :

PLATELET COUNT :

LIVER FUNCTION TEST :

FUNDUS EXAMINATION :

USG:

DOPPLER (WHEREVER INDICATED) :

ABBREVIATIONS

BP	-	Blood Pressure
EDD	-	Expected Date of Delivery
HELLP	-	Hemolysis, Elevated Liver enzmes Low Platelet
IUGR	-	Intra Uterine Growth Retardation
LDH	-	Lactate dihydrogenase
LMP	-	Last Menstrual Period
P value	-	Probability value
PCR	-	Protein to Creatinine Ratio
POG	-	Period of Gestation
r	-	Pearson's Correlation Coefficient
SD	-	Standard Deviation
SE	-	Standard Error
SGOT	-	Serum Glutamate Oxaloacetate Transaminase
SGPT	-	Serum Glutamate Pyruvate Transaminase
USG	-	Ultrasonogram
UTI	-	Urinary Tract Infection

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S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
1	31	G2P1L1	150	90	36	3+	4000	8.8	
2	23	PRIMI	160	110	27	3+	5250	2.3	
3	27	G2A1	140	90	37	3+	3250	5.2	
4	23	PRIMI	140	96	35	3+	3366	3.9	
5	18	PRIMI	160	100	25	3+	3270	2.2	Grade II HT Retinopathy
6	25	G3P2L1	140	100	27	4+	5800	1.72	
7	24	PRIMI	150	94	36	3+	3190	1.7	
8	20	PRIMI	150	110	27	4+	7800	8.2	
9	24	PRIMI	150	90	36	3+	3000	2.5	
10	27	PRIMI	150	100	34	3+	3600	11.39	
11	25	PRIMI	140	90	38	3+	2310	3.5	
12	23	PRIMI	140	94	36	3+	1120	1.83	
13	22	PRIMI	150	90	36	4+	1546	3.4	
14	20	G2P1L1	160	100	33	3+	1454	3.11	Recurrent Preeclampsia
15	31	PRIMI	140	90	36	3+	1220	0.98	
16	23	PRIMI	150	100	33	4+	1840	3.32	

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
17	22	G2P1L0	150	110	34	3+	1176	1.02	IUGR, Rec. Preeclampsia
18	26	PRIMI	140	90	36	3+	1020	2.12	
19	20	PRIMI	160	100	32	2+	2546	2.2	
20	31	G2A1	160	90	39	1+	963	1.2	
21	30	PRIMI	160	100	33	1+	631	0.76	
22	32	G2P1L1	150	110	38	3+	984	1.02	
23	28	PRIMI	140	110	34	1+	756	0.92	
24	31	PRIMI	170	100	33	1+	640	0.58	Grade II HT Retinopathy
25	29	PRIMI	160	104	35	1+	386	0.4	
26	29	G2P1L1	160	90	38	1+	482	0.52	
27	20	G2P1L1	150	110	34	1+	570	0.48	
28	27	G3P1L1A1	160	96	36	2+	960	1.4	
29	19	PRIMI	140	110	32	1+	824	1.2	
30	19	PRIMI	160	90	37	1+	1140	2.12	
31	21	PRIMI	160	100	34	1+	874	1.12	
32	32	PRIMI	160	100	34	2+	1134	0.98	
33	23	G2P1L1	140	90	39	1+	420	0.81	IUGR

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
34	18	PRIMI	150	110	34	2+	824	0.77	
35	24	G2P1L1	140	110	33	2+	740	0.76	
36	25	G2A1	170	90	36	1+	524	0.66	
37	18	PRIMI	170	90	36	1+	840	0.92	
38	19	PRIMI	160	110	26	2+	920	1.1	
39	18	PRIMI	160	100	38	2+	560	0.68	PP Eclampsia
40	21	PRIMI	160	100	35	1+	840	1.32	
41	19	PRIMI	150	110	33	2+	767	1.01	
42	23	PRIMI	150	100	34	2+	1320	2.56	IUGR
43	20	G2P1L1	160	90	36	1+	760	0.92	
44	22	PRIMI	150	110	35	2+	640	0.81	
45	35	PRIMI	160	100	35	1+	520	0.61	
46	23	PRIMI	140	110	37	2+	970	2.1	
47	22	PRIMI	140	110	34	2+	848	0.96	
48	31	G3P2L0	140	100	36	2+	340	0.18	IUGR, Rec. Preeclampsia
49	26	G2P1L1	160	110	32	2+	980	1.45	
50	31	PRIMI	130	94	36	2+	1324	2.2	IUGR

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
51	18	PRIMI	150	80	30	1+	356	0.41	
52	25	G3P1L1A1	150	94	38	2+	1370	2.1	PP Eclampsia
53	20	PRIMI	140	90	39	2+	878	0.76	IUGR
54	34	G3P2L1	150	80	27	1+	422	0.63	
55	33	G3P2L1	150	90	39	2+	1140	1.45	IUGR
56	31	G2P1L1	140	90	37	1+	550	0.48	
57	31	G2P1L1	130	100	38	1+	448	0.48	
58	31	PRIMI	150	90	39	1+	720	0.8	
59	33	G2P1L1	140	90	27	1+	325	0.32	
60	19	PRIMI	140	90	39	1+	960	1.2	PP Eclampsia
61	32	G2P1L1	150	90	40	1+	548	0.82	
62	32	G2P1L0	150	100	37	1+	842	1.32	Recurrent Preeclampsia
63	19	PRIMI	130	100	38	2+	1323	2.1	
64	18	PRIMI	140	90	34	1+	776	0.74	
65	20	G2P1L1	150	90	34	1+	645	0.89	
66	19	PRIMI	150	90	33	1+	440	0.74	
67	27	PRIMI	140	90	35	1+	732	0.59	IUGR

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
68	20	G2P1L1	150	90	34	1+	648	0.48	
69	19	PRIMI	150	80	30	1+	572	0.67	
70	18	PRIMI	130	100	36	2+	1154	1.72	
71	20	G2P1L1	150	90	35	1+	476	0.52	
72	19	PRIMI	150	100	36	2+	996	1.32	
73	19	PRIMI	140	100	36	1+	760	0.82	
74	18	PRIMI	150	84	34	1+	376	0.51	
75	19	G3P1L1A1	140	100	36	2+	292	0.37	
76	20	PRIMI	140	96	37	1+	960	1.8	
77	20	PRIMI	130	96	38	1+	320	0.36	
78	19	PRIMI	140	86	34	1+	700	0.88	
79	18	PRIMI	150	90	38	1+	640	0.46	
80	20	PRIMI	140	86	37	1+	348	0.28	
81	20	PRIMI	140	100	36	2+	870	1.23	
82	19	PRIMI	150	94	40	1+	135	0.16	
83	22	G2P1L1	130	100	25	1+	138	0.19	
84	27	PRIMI	140	90	38	1+	742	0.96	

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
85	26	PRIMI	130	90	26	1+	198	0.2	
86	24	G2P1L1	140	86	39	1+	380	0.43	
87	24	G2P1L1	140	100	36	1+	476	0.53	
88	23	PRIMI	150	90	36	1+	560	0.61	
89	28	G3P2L2	150	80	33	1+	154	0.19	
90	21	PRIMI	150	94	38	1+	254	0.29	
91	30	G3P2L1	140	90	32	1+	200	0.21	
92	22	G2P1L1	130	96	34	1+	285	0.37	
93	25	PRIMI	150	90	35	1+	220	0.25	
94	25	PRIMI	154	90	35	1+	576	0.67	
95	26	G3P1L1A1	140	86	36	1+	220	0.24	
96	26	PRIMI	140	90	35	1+	530	0.76	
97	26	G2P1L1	150	94	37	2+	3550	1.9	Recurrent Preeclampsia
98	24	PRIMI	150	100	36	2+	1220	1.52	
99	23	PRIMI	130	100	37	1+	970	0.84	
100	22	PRIMI	140	94	37	1+	135	0.16	
101	21	PRIMI	140	86	38	1+	221	0.93	

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
102	28	G2P1L1	140	100	37	2+	1030	1.8	
103	23	PRIMI	130	94	37	2+	1190	1.6	
104	29	G2P1L1	130	90	29	1+	236	0.22	
105	24	PRIMI	140	90	37	1+	530	0.28	
106	21	G2P1L1	150	100	36	2+	766	0.92	
107	29	PRIMI	154	90	37	1+	480	1.04	
108	24	G2P1L1	144	80	38	1+	320	0.41	
109	24	PRIMI	140	90	38	2+	851	1.2	
110	26	PRIMI	130	90	28	1+	420	0.39	
111	27	PRIMI	140	80	29	2+	544	0.76	
112	25	PRIMI	150	84	37	1+	480	0.46	
113	24	G2P1L1	130	100	37	1+	424	0.57	
114	23	PRIMI	140	90	38	2+	880	1.19	
115	21	G2P1L1	150	84	35	1+	490	0.76	
116	25	PRIMI	150	90	36	1+	490	0.52	
117	29	G3P1L1A1	136	90	38	1+	670	0.88	
118	26	G2P1L1	140	94	37	1+	250	0.27	

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
119	28	G2P1L1	140	100	35	2+	842	1.1	
120	24	G3A2	140	90	36	1+	860	1.3	
121	30	G3P2L1	130	96	37	2+	821	1.1	
122	23	PRIMI	140	90	37	1+	525	0.6	
123	27	PRIMI	130	90	27	1+	235	0.31	
124	22	G2P1L1	130	94	39	1+	240	0.2	
125	21	PRIMI	150	90	37	1+	376	0.42	
126	27	G2P1L0	140	100	35	1+	476	0.61	
127	30	G3P1L0A1	150	100	36	2+	1450	2.42	Recurrent Preeclampsia
128	37	G3P2L2	140	80	26	1+	180	0.17	
129	26	PRIMI	150	80	27	1+	176	0.18	
130	26	G3P2L2	140	90	34	1+	676	0.89	
131	23	G2P1L1	150	90	35	1+	490	0.57	
132	21	G2P1L1	130	94	35	2+	978	1.2	
133	0	PRIMI	130	90	27	1+	145	0.13	
134	22	PRIMI	140	94	36	2+	1170	1.52	
135	23	G2P1L1	130	94	39	1+	842	1.43	

S. No.	AGE	PARITY	SYS BP	DIA BP	GES AGE	DIPSTICK	24 HUP	SPOT PCR	REMARKS
136	25	PRIMI	150	86	34	1+	456	0.67	
137	28	G2P1L1	140	90	34	1+	620	0.77	
138	27	G2P1L1	130	90	36	1+	188	0.19	
139	26	PRIMI	150	90	39	1+	450	0.39	
140	26	G2P1L1	140	90	24	1+	235	0.22	
141	25	PRIMI	130	90	40	1+	176	0.19	
142	24	G2A1	140	86	33	1+	200	0.19	
143	24	PRIMI	150	86	34	1+	242	0.3	
144	22	PRIMI	150	94	25	1+	240	0.27	
145	21	G2P1L1	140	90	34	1+	268	0.31	
146	30	G3P1L1A1	130	90	34	1+	272	0.25	
147	21	PRIMI	130	90	24	1+	132	0.15	
148	28	G2P1L1	150	84	33	1+	276	0.31	
149	26	G2P1L1	144	84	33	1+	290	0.42	
150	25	G2P1L1	140	90	35	1+	186	0.16	